

Untreated Syphilis in the Male Negro

Twenty-Two Years of Serologic Observation in a Selected Syphilis Study Group

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Since 1932 there has been carried on a study of the outcome of untreated syphilis in the male Negro.* Although the primary objective of this study is the determination of the clinical outcome, this group of patients also furnishes valuable data on the serologic pattern of untreated syphilis.

No serologic data are available for the period from the initial examination in 1932-1933 to the first follow-up examination in 1938-1939. Since 1939, however, annual serologic examinations have been attempted. The last examination, completed in December, 1954, extended the observation period

Submitted for publication Nov. 9, 1955.

This article is one of a series on untreated syphilis in the male Negro which the Venereal Disease Program, Division of Special Health Services, plans to assemble into a monograph. Single copies of the monograph will be made available upon request to the Venereal Disease Program, Division of Special Health Services, Public Health Service, U. S. Department of Health, Education, and Welfare, Washington 25, D. C.

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to 22 years. The initial serologic examination in 1932-1933 was based on the Kolmer complement fixation and Kahn standard flocculation tests for syphilis, performed at the National Institute of Health. For the 1938-1939 and subsequent surveys serologic testing has been done by the Venereal Disease Research Laboratory (formerly at Staten Island, N. Y., and now located at Chamblee, Ga.). Although a battery of tests has been employed, the Kahn standard is the only test remaining more or less constant throughout the 22 years of observation. The following analysis, except for a comparison of tests employed in the most recent surveys, will be limited, therefore, to results obtained by the Kahn technique.

In addition to the 408 men selected as syphilitic in 1932-1933, this analysis includes 10 of the 201 nonsyphilitic controls selected in 1933-1934 who later acquired syphilis and 13 of the 14 syphilitic patients added to the study in 1938-1939. The 14th patient in this latter group has been omitted because of questionable history of infection and large amount of antisyphilitic treatment received. Thus, the syphilitic group under consideration totals 431 men.

The status of these patients as of December, 1954, is shown in Table 1 by duration of infection on admission to the study. Of the 431 men, 176 (40.8%) were known to be dead. The death rate increased from 18% among patients with syphilis of less than 10 years' duration to 96% among patients with syphilis of 40 or more years' duration at time of admission to the study. These seemingly high death rates are attributable to the fact that 56% of the patients were over 40 years of age at the time of selection; 30%, over 50 years of age.

TABLE 1.—Status of Patients as of December, 1954

Duration of Infection on Admission to Study (Years)	Total	Known Dead		Presumed Living		Examined in 1954	
		Number	Per Cent	Number	Per Cent	Number	Per Cent of Living
0-4.....	69	14	20.6	54	79.4	16	29.6
5-9.....	84	14	16.7	70	83.3	12	17.1
10-14.....	55	22	40.0	33	60.0	13	39.4
15-19.....	48	20	41.7	28	58.3	13	46.4
20-24.....	40	20	50.0	20	50.0	9	45.0
25-29.....	47	25	53.2	22	46.8	10	45.5
30-34.....	40	22	55.0	18	45.0	10	55.6
35-39.....	23	14	60.9	9	39.1	9	100.0
40-44.....	14	13	92.9	1	7.1	1	100.0
45-49.....	5	5	100.0	..	0.0	..	0.0
50+.....	7	7	100.0	..	0.0	..	0.0
Total.....	431	176	40.8	255	59.2	93	36.5

Only 93 patients, or 36.5% of those presumed to be alive, were examined in 1954. The percentage examined was lowest in patients with syphilis of less than 15 years' duration, owing principally to the fact that more of the younger patients have moved from the area. The 10 patients presumed to be alive in spite of the fact that syphilis was of 35 or more years' duration at time of selection were all examined in 1954, their ages ranging at that time from 75 to 81 years.

Of the total group of 431 syphilitic patients, 299 have had serologic follow-up. In 29 patients this was limited to the examination in 1938-39. However, 183 have been examined serologically since 1951. Seventy-six patients died before they could be reexamined and the remaining fifty-six were lost from observation. On the basis of modern standards the patients included in this study have been considered "untreated." However,

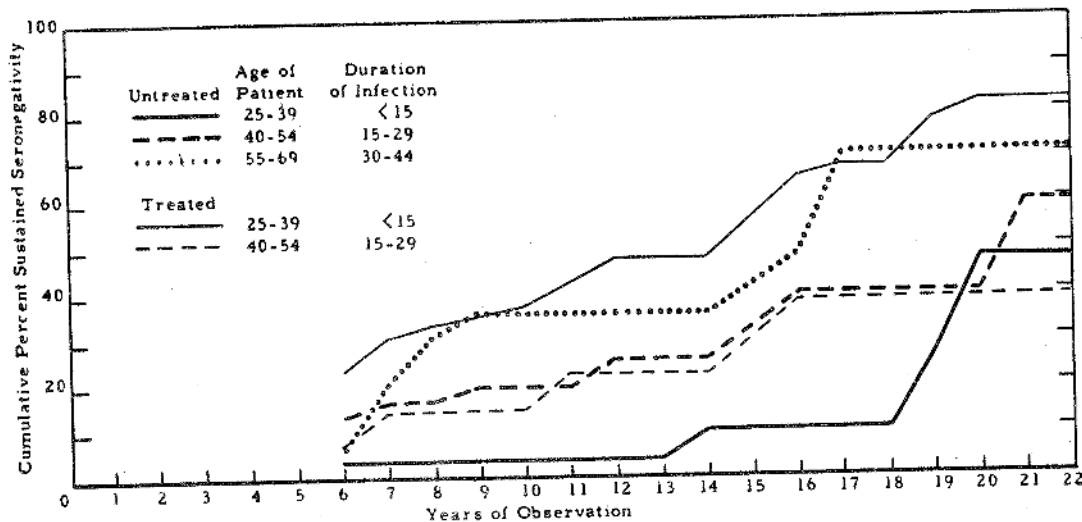
the majority have received some form of inadequate antisyphilitic treatment. The duration of infection on admission to the study and the amount of treatment received prior to the first follow-up examination is shown in Table 2 for the 299 patients serologically examined. Thirty-eight patients were completely untreated and an additional 137 were treated with heavy metal (almost exclusively mercury) or less than three arsenical injections. These two groups have been considered "untreated" in the following discussion. One hundred seventeen were treated with 3 to 11 arsenical injections, and eight with more than this amount. In general, those receiving the most treatment were patients with syphilis of shortest duration.

According to the Sing Sing criteria¹¹ used in previous papers of this series, all but 8 of the 299 patients would be considered "untreated." However, the effect on serologic

TABLE 2.—Treatment Prior to First Follow-up Examination

Duration of Infection on Admission to Study (Years)	Cases with Serologic Follow-Up	Treatment Prior to First Follow-up Examination							
		None		Less than 3 Arsenic or Heavy Metal Only		3-11 Arsenicals		12 or More	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
0-4.....	57	12	21.1	11	19.3	30	52.6	4	7.0
5-9.....	53	3	5.5	13	23.6	38	69.1	1	1.8
10-14.....	35	5	14.3	8	22.9	21	60.0	1	2.8
15-19.....	38	2	5.3	21	55.2	15	39.5	..	0.0
20-24.....	19	1	5.3	14	73.7	4	21.0	..	0.0
25-29.....	32	5	15.6	19	59.4	7	21.9	1	3.1
30-34.....	29	4	13.8	24	82.8	1	3.4	..	0.0
35-39.....	19	2	10.5	16	84.2	..	0.0	1	5.3
40-44.....	10	4	40.0	6	60.0	..	0.0	..	0.0
45-49.....	2	..	0.0	2	100.0	..	0.0	..	0.0
50+.....	3	..	0.0	3	100.0	..	0.0	..	0.0
Total.....	299	38	12.7	137	45.8	118	39.3	8	2.7

Figure 1. Influence of duration of infection on rate of seroreversal in treated and untreated patients.



reversal of even the small amount of treatment administered to the patients in this study is illustrated in Figure 1. For this reason the "untreated" group is limited to patients receiving less than three arsenical injections. Since some patients received treatment subsequent to the first follow-up examination, in calculating seronegativity rates serologic observation has been terminated at the time this additional treatment was given.

In untreated syphilis, serologic reversal to negative is principally a function of time.

Theoretically, therefore, spontaneous reversal would occur in all patients if the life span could be sufficiently extended. It follows, then, that, the more recently acquired the infection, the longer the time required for reversal to negative. This is borne out by the pattern of the cumulative seronegativity curves presented in Figure 1. In untreated syphilis (represented by heavy lines), the lowest reversal rate was observed among patients 25-39 years of age with syphilis of less than 15 years' duration (solid line). The highest reversal rate was observed

TABLE 3.—Estimated Death Rate Among Untreated Syphilitic Negro Males by Duration of Infection

Duration of Infection (Years)	a Number Admitted to Study	b Survivors from Previous Duration-Interval $c_{n-1} + d_{n-1}$	c Total in Duration-Interval $c_n + d_n$	d Dead or Lost	e Adjusted Number in Duration-Interval $100 \frac{c_n}{c_n + d_n}$	Dead			
						f Number	g Per Cent $\frac{f_n}{c_n}$ 100	h Cumulative Per Cent $g_1 + g_2 + \dots + g_n$	i Per Cent Living 100-h
0-4.....	29	..	29	1	29	1	3.4	3.4	96.6
5-9.....	26	28	54	2	56	2	3.6	7.0	93.0
10-14.....	24	52	76	9	82	7	8.5	15.5	84.5
15-19.....	26	67	96	19	114	9	7.9	23.4	76.6
20-24.....	32	77	109	16	142	7	4.9	28.3	71.7
25-29.....	39	93	132	35	164	18	9.8	38.1	61.9
30-34.....	39	97	136	33	220	18	8.2	46.3	53.7
35-39.....	22	108	125	28	233	14	6.0	52.3	47.7
40-44.....	14	97	111	60	233	13	5.6	57.9	42.1
45-49.....	5	81	86	87	204	26	12.7	70.6	29.4
50-54.....	4	49	53	83	180	18	7.2	77.8	22.2
55-59.....	..	20	20	12	90	3	3.3	81.1	18.9
60-64.....	2	8	10	7	58	3	5.7	86.8	13.2
65-69.....	..	8	3	1	23	1	4.3	91.1	8.9
70-74.....	1	2	3	2	24	2	5.9	97.0	3.0
75-79.....	..	1	1	1	33	1	3.0	100.0	0.0

among patients 55-69 years of age with syphilis of 30-44 years' duration (dotted line). The dashed line, representing patients 40-54 years of age with syphilis of 15-29 years' duration, falls approximately midway between the two.

The administration of only a small amount of treatment, however, reverses this pattern (thin lines). Patients 25-39 years of age with syphilis of less than 15 years' duration (solid line) when treated with 3-20 arsenical injections had the highest seronegativity rate. The same amount of treatment administered to patients 40-54 years of age with syphilis of 15-29 years' duration had no apparent effect (dashed line). The seronegativity curve for treated syphilis was practically identical with the curve for untreated syphilis in the same age group and with the same duration of infection.

Unlike the Bruusgaard study of untreated syphilis¹² in which all patients had early infectious syphilis at time of selection, the Tuskegee study has no base line, or starting point. The duration of syphilis at the time patients were selected for study varied from a few months to 72 years. However, at the time of the initial examination the syphilitic group was considered a representative sample of untreated seropositive syphilis in the male Negro.¹ Presumptive evidence of uncomplicated aortitis was found at that time in 23.6%, definite clinical evidence of central nervous system syphilis in 7.8%, central nervous system involvement based only upon spinal fluid findings in 18.3%, and evidence of late involvement of the bones, joints, and skin was present in 11.5%. And, to quote the examining physician, "In order to be certain that there was no selection of cases through loss to institutions for the insane, it was learned that not a single male Negro over 25 years of age was confined with syphilis of the central nervous system in the Searcy Hospital at Mt. Vernon, Alabama, where the Negro insane in this State are hospitalized."

It seems fair to assume, then, that patients with a given duration of infection on admission to the study are representative of

TABLE 4.—Estimated Seronegativity Rate Among Untreated Syphilitic Negro Males by Duration of Infection

a	b	c	d	e	f	g	h	i	j	k	Per Cent Living		m
											Negative No. ka 100	Positive No. ka 100	
Duration of Infection (Years)	Number Admitted to Study	Positives from Previous Duration- Interval Ca-2-da-1	Total in Duration- Interval Na+ba	Negative or Lost	Adjusted Number in Duration- Interval 100 ea	Number	Per Cent Negative 100 fa	Cumulative Per Cent g1+g2+...+ga	Per Cent Positive 100 ha	Total (Col. 1 Table 3)			
0-4	23	..	23	7	23	2	8.7	..	91.3	96.6
5-9	23	..	23	6	35	4	11.4	8.7	79.9	93.0	8.1	84.9	..
10-14	16	16	32	10	49	8	6.1	20.1	73.8	84.5	17.0	67.5	..
15-19	13	26	39	18	70	9	12.9	26.2	60.9	76.8	20.1	53.6	..
20-24	23	29	52	22	80	11	13.9	39.1	47.1	71.7	28.0	43.7	..
25-29	15	34	49	13	108	4	3.7	56.6	43.4	61.9	32.7	29.2	..
30-34	24	27	51	23	152	8	5.3	61.9	38.1	53.7	30.4	23.3	..
35-39	23	33	56	20	160	96	3.8	65.7	34.3	47.7	29.5	18.2	..
40-44	18	43	61	23	149	15	10.1	75.8	24.2	42.1	27.7	14.4	..
45-49	10	51	61	16	103	6	5.8	81.6	18.4	29.2	18.1	4.1	..
50-54	2	25	25	8	54	2	3.7	95.3	14.9	18.9	16.1	2.8	..
55-59	1	10	10	2	14	1	7.1	92.4	7.3	13.2	12.3	1.0	..
60-64	..	1	1	..	13	..	0.0	92.4	7.3	8.9	8.2	0.7	..
65-69	1	1	1	1	13	..	0.0	92.4	7.3	8.0	2.9	0.3	..
70-74	..	1	1	..	13	..	0.0	92.4	7.3	0.6	0.0	0.0	..
75-79	1	..	1	..	13	..	0.0	92.4	7.3	0.6	0.0	0.0	..

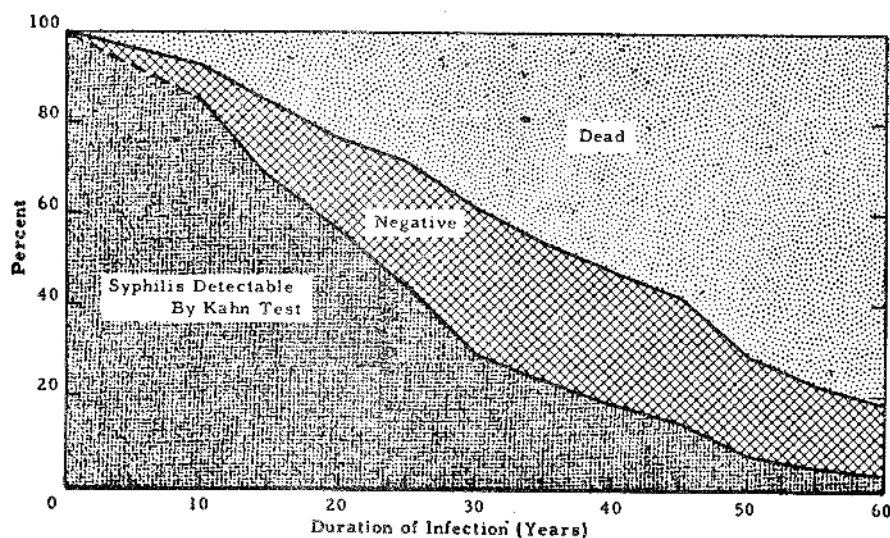
patients acquiring syphilis who have survived and have remained seropositive for that period of time. In other words, the assumption is made that persons entering the study with a particular duration of infection are a segment of a group who had the same mortality and serologic reversal experience as those observed in earlier periods.

The statistical method employed in estimating the death rate and rate of serologic reversal to negative in untreated syphilis is shown in Tables 3 and 4. Appropriate adjustments have been made in column e for deaths and reversals that occurred in previ-

remains untreated, by 20 years after infection approximately 23% of Negro males will have died, 20% will have reverted to negative, and 57% will still be positive. By 30 years following infection, 38% will have died, 33% will have reverted to negative, and 29% will still be positive; that is, by 30 years after infection, in less than 50% of those surviving will syphilis be detectable by the Kahn test.

The high death rate shown in Figure 2 is explained in part by the selection for study of patients 25 years of age or older. However, as was discussed in a previous paper

Figure 2. Estimate of serologic status of untreated syphilitic male Negroes by years after infection.



ous intervals. As stated previously, the first follow-up examination was performed six years after the study was initiated. It is unknown, therefore, how many patients with syphilis, for example, of 0.4 years duration reversed to negative within 5 years after infection. For this reason, patients with syphilis of 0.4 years' duration are first included in Table 4 in the 5-9-year period, patients with syphilis of 5-9 years' duration are first included in the 10-14-year period.

The death and seronegativity curves derived from Tables 3 and 4 are presented in Figure 2. The unknown portion of the seronegativity curve is shown by the dashed line. These estimates indicate that, if syphilis

of this series,⁵ untreated syphilis reduces life expectancy by approximately 17% in Negro males between the ages of 25 and 50. The estimate of seronegativity is higher, of course, than it would be if based on an STS more sensitive than the Kahn. For example, in the 1953 or 1954 surveys, 72 of these untreated patients were tested by the Kahn, Kolmer, VDRL, and TPI techniques. The percentage nonreactive was about the same for the Kahn and VDRL tests, 53 and 56%, respectively. Only 40%, however, were nonreactive to the Kolmer test, 25% less than to the Kahn test.

Of the 72 patients 4 were nonreactive to the TPI test. Only one of these patients

was positive serologically both at time of selection and again at the first follow-up examination. Certainly there is little evidence in this group of patients to indicate that the TPI test in untreated syphilis becomes negative with the passage of time. The duration of syphilis at the time of the TPI examinations ranged from 14 to 63 years. In the four patients with negative TPI tests, the duration of infection was 34, 42, 47, and 50 years. Twenty-four patients with syphilis of more than 50 years' duration were all reactive to the TPI test.

TABLE 5.—Status as Determined by Physical Examination or Autopsy of Patients Who Had Spontaneous Reversal of Kahn Test to Negative

	Number	Per Cent
Physical examination	43	100.0
Clinically negative	86*	88.7
Cardiovascular syphilis	5	11.6
Aortic insufficiency	3	7.0
Aneurysm	2	4.7
Neurosyphilis	1	2.3
Tabes and optic atrophy	1	2.3
Osseous syphilis (gumma of palate) ..	1	2.3
Postmortem examination	19	100.0
Negative for syphilis	9	47.4
Cardiovascular syphilis	8	42.1
Gross examination only	5	26.3
Microscopic examination only	4	21.1
Syphilitic osteitis of calvarium	1	5.3
Total living and dead	62	100.0
Negative for syphilis	46*	72.6
Cardiovascular syphilis	14	22.6
Neurosyphilis	1	1.6
Osseous syphilis	2	3.2

* Includes 11 patients with possible uncomplicated aortitis.

That spontaneous seroreversal is not synonymous with spontaneous cure is apparent from Table 5, which shows the results of physical examination or autopsy for 62 of the patients in whom the Kahn test reverted to negative without treatment. Seventeen patients, 27%, had clinical evidence of late syphilis. This is a minimum figure, since possible uncomplicated aortitis has not been included. Cardiovascular syphilis was diagnosed in 14 patients, neurosyphilis (tabes with optic atrophy), in 1, and osseous syphilis in 2.

Eighty-four per cent of the living patients were clinically negative for syphilis as compared with forty-seven per cent of those who

came to autopsy. This may reflect the difference in age of the two groups, since the living patients were an average of 5 years younger than the dead. It is also possible that some of the uncomplicated aortitis disregarded in the living may have been of syphilitic origin.

SUMMARY AND CONCLUSIONS

An analysis of 22 years of serologic observation by means of the Kahn test of patients included in the Tuskegee study is presented.

In untreated syphilis, the percentage reversing to negative by the Kahn test was lowest in patients 25-39 years of age with syphilis of less than 15 years' duration; highest in patients 55-69 years of age with syphilis of 30-44 years' duration.

A small amount of treatment (3-20 arsenical injections) administered to patients 25-39 years of age with syphilis of less than 15 years' duration influenced the serologic course; treatment administered later was of no apparent benefit in producing seronegativity.

It is estimated that less than 50% of untreated syphilis in male Negroes will be detectable by the Kahn technique 30 years after infection.

There is no evidence to indicate that the TPI test in untreated syphilis becomes non-reactive with the passage of time.

Twenty-seven per cent of patients with spontaneous serologic reversal had clinical manifestations of late syphilis.

There is variability in the pattern of seroreversal in untreated syphilis just as in treated syphilis.

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